In the specification:

Replace the paragraph on page 5, lines 14-25 with the amended paragraph below:

A method for protein design has been described by Miller and coworkers (U.S. Patent Application Serial No. 09/730,214, incorporated herein by reference) in which backbones are generated as a sequence of particular pairs of dihedral angles. All backbone configurations which can be made from a chosen set of dihedral angle-pairs are generated. In order to generate a sufficient variety of configurations, the number of pairs of dihedral angles must be at least 3. The number of configurations generated is therefore at minimum ~~3^N~~ 3^N, where N is the number of amino acids in the chain. This exponential growth of the number of configurations with the length of the chain limits the method to chains of fewer than thirty amino acids, given current computational limits.

Replace the paragraph on page 6, lines 19-25 with the amended paragraph below:

Thus, backbone configurations employed to date have either been taken directly from nature, or are slight modifications of natural configurations, or are limited to chains of fewer than thirty amino acids. ~~The ability to identify foldable backbone configurations of new protein folds.~~ Thus, there exists a need in the art to identify new designable protein structures, particularly for chains of more than thirty amino acids.

Replace the paragraph on page 8, lines 1-4 with the amended paragraph below:

Figure 3 Illustrates four of the most designable four-helix folds. Figure 3(a) is an up and down fold. Figure 3(b) is an up and down with a cross-over connection fold. Figure 3(c) is ~~an~~ a λ repressor-type fold. Figure 3(d) is an orthogonal array fold.

Replace the paragraph on page 17, lines 4-27 with the amended paragraph below:

For the designability calculation, binary sequences consisting of only two types of amino acids are employed. Such sequences are known as "HP-sequences", for hydrophobic (H) and polar (P) amino acids. In accordance with the present invention, a random sequence of amino acids can have a length of 2^n, where n=1-500. The two hydrophobicity values are $h_i = h_0 \pm \delta h$, where h_0 is a compactification energy, and δh measures the relative distance between hydrophobic and polar residues. Using the Miyazawa-Jernigan matrix (S. Miyazawa and R.L. Jernigan (1985) Macromolecules 18:534; S. Miyazawa and R.L. Jernigan (1996) J. Mol Biol 256:623, incorporated herein by reference)~~, incorporated herein by reference,~~ of amino acid interaction energies, a typical energy difference between hydrophobic and polar residues is inferred to equal $1.5k_BT$/contact. On average, a buried residue makes four non-covalent contacts. Therefore $2\delta h = 6.0\ k_BT$. The compactification energy, h_0, is determined by fitting the surface-area distribution of a set of natural m-element bundles to the surface-area distributions for the 50-1000 most designable m-element-stacks, wherein m=1-20, using different values of h_0 to assess designability. In one embodiment, h_0, is determined by fitting the surface-area distribution of a set of natural four-helix bundles to the surface-area distributions for the 100 most designable

four-helix-stacks, using different values of h_0 to assess designability. The best fit preferably corresponds to $h_o = 2k_BT$ and hydrophobic residues have a hydrophobicity of $5k_BT$ and polar residues $-1k_BT$.

Replace the paragraph on page 23, lines 3-27 with the amended paragraph below:

All of the designable stacks fall within one of four folds, and these are shown in order of designability rank in Fig. 3. A metric based on helical directions was used to determine that all of the representative structures with a designability greater than 100 fall within approximately 15°/helix of one of these four ~~folds)~~ folds. The topmost designable structure is an up-and-down four-helix bundle. The second most designable fold is a variant of the up-and-down fold except that there is a crossover connection. The third most designable fold falls within the λ repressor-like DNA-binding domain class. The last fold is an orthogonal array. Table II presents binary sequences which have these structures as lowest energy folds. These particular sequences were calculated by matching them to the surface area pattern of each of the four folds and then performing a simple energy gap optimization. The energy of optimization was done by first calculating the mean surface area exposure of each side chain for each structure. For a given structure, the sequence was then assigned by putting hydrophobic residues on sites which had surface exposures below the mean and polar residues on those sites whose exposure exceeded the mean. The energy gap optimization was then performed. The energy gap was defined to be the energy difference between the ground state energy and the first excited state ~~that~~ at a rms greater than 4 Angstroms (i.e. a structure that is significantly different than the ground state).

Point mutations were randomly performed on the sequence by changing an H to a P or a P to an H, and the mutation was maintained if it made the gap larger.

Replace the legend to Table II, the last three lines on page 24 and first two lines on page 25, with the amended legend below:

Results for the top four distinct designable folds for the model four-helix bundles shown in Fig. 3. Column 2 gives the hydrophobic-polar patterning of each of the length-15 helices. The last column gives the energy gap in kT between the structures and their nearest distinct structural competitor.